

UNITED STATES PATENT & TRADEMARK OFFICE

**Examiner:** DUNSTON, JENNIFER ANN

**Applicant :** CHOI *et al.*

**Application No.** 10/597,305

**Filed:** July 19, 2006

**For:** DIFFERENTIATION REGULATING AGENT CONTAINING GENE WHICH  
REGULATING DIFFERENTIATION FROM STEM CELLS INTO NATURAL  
KILLER CELLS AS EFFECTIVE INGRADIENT

**Art Unit:** 1636

**Attorney Docket No.:** 58049-00034

COMMISSIONER FOR PATENTS

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**DECLARATION UNDER 37 C.F.R. §1.132**

I, CHOI, Inpyo am a main inventor named in the above-referenced patent application.

I, CHOI, Inpyo declare and state:

1. My educational background includes Ph.D. in the field of Ph.D. in the field of molecular biology Dept of Biology from University of Alabama, Alabama, USA, MS in biological science Dept of College of Natural Science, Seoul, Korea, and BS in biological science Dept of College of Natural Science, Seoul, Korea.

2. I worked as Director, Stem Cell Research Center, Research Institute of Bioscience and Biotechnology (KRIBB), Taejeon-si, Korea, from 2006 to 2008. I also worked as Director, Cellomics Research Center, Research Institute of Bioscience and Biotechnology (KRIBB), from 2003.5 to 2005. I also worked as Head in Laboratory of Immunology, Research Institute of Bioscience and Biotechnology (KRIBB), from 1996.3 to 2003.5. I also worked as Senior Researcher, Research Institute of Bioscience and Biotechnology (KRIBB), from 1991 to 1996.2. I also worked as Postdoctoral Fellow in Medical College of Virginia, Virginia Commonwealth University, Virginia, USA, from 1988 to 1991.
3. I presently hold the position of Director, Cell Therapy Research Center, Research Institute of Bioscience and Biotechnology (KRIBB), Taejeon-si, Korea.
4. I am an expert in the field of Cell therapy and Immunology. I am also a member of American Association of Immunologist, International Society of Cytokines, Korean Society for Immunology and Korean Society of Molecular Biology.
5. My further professional experience, publications are summarized by my Curriculum Vitae, which is attached as Exhibition A.
6. Even though I disclosed the specification of the present invention, I have done experiments to confirm function of genes. Especially, in order to confirm whether pNK-specific expression of Ferritin H was required for the differentiation into mNK,

HSC cells were cultured for 6 days, which were then treated with IL-5 and Ferritin H in the absence of OP9 stromal cells, followed by measuring the percentage of NK cells.

7. I finally found effects of Ferritin H on the NK cell. As described in supplementary figure, when HSC was treated with IL-15 and Ferritin H together, percentage of the NK cell was increased more than that when it was treated with IL-15 only (NK1.1+ cell; 14% treated with IL-15 only versus 23% treated with IL-15 and 1 ug/ml of Ferritin H together, and NK1.1+ NKG2A/C/E+ cell; 39% treated with IL-15 only versus 43% treated with IL-15 and 1 ug/ml of Ferritin H together). The above results indicate that Ferritin H plays an important role in the differentiation from pNK cells into mNK cells and the search of genes regulating NK cell differentiation was correctly done in the present invention.

8. I further declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful and false statements and like so made are punishable by fine or imprisonment, or both, under '1001 of Title 18 of the U.S. Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

July 16, 2009

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CHOI, Inpyo

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Date

Exhibit A

Patent Application (**Domestic**)

1. Korean Patent No.: 10-0161145-0000 (1998.08.21)

Title: PHARHACEUTICAL COMPOSITIONS CONTAINING EXTRACTS OF STEPHANIA TETRANDRAS MOORE USING FOR INHIBITING THE PRODUCTION OF INTERLEUKIN-6

2. Korean Patent No.: 10-0145941-0000 (1998.05.06)

Title: PHARHACEUTICAL COMPOSITIONS CONTAINING ACANTHOIC ACID FOR INHIBITING PRODUCTION OF INTERLEUKIN-1 AND TNF-ALPHA. ACANTHOIC **ACID**

3. Korean Patent No.:10-0204504-0000 (1999.03.29)

Title: PROCESS FOR THE PRODUCTION OF HUMAN INTERLEUKIN-6 USING YEAST

4. Korean Patent No.: 10-0210512-0000 (1999.04.27)

Title: HUMAN INTERLEUKIN-6 ANTIBODY AND IDENTIFICATION OF HUMAN INTERLEUKIN-6 BY USING THE SAME

5. Korean Patent No.: 10-176419-0000 (1998.11.13)

Title: PROCESS FOR THE PREPARATION OF SOLUBLE HUMAN INTERLEUKIN-6

6. Korean Patent No.:10-229419-0000 (1999.08.16)

Title: MUTANT HUMAN INTERLEUKIN-6

7. Korean Patent No.:10-0250835-0000 (2000.01.07)

Title: HYBRIDOMA AND ITS MONOCLONAL ANTIBODY CONTROLLING THE FUNCTION OF HUMAN NATURAL KILLER CELL

8. Korean Patent No.:10-0250836-0000 (2000.01.07)

Title: HYBRIDOMA AND ITS MONOCLONAL ANTIBODY RECOGNIZING HUMAN STROMAL CELL OF BONE MARROW AND CONTROLLING PROLIFERATION AND DIFFERENTIATION OF B LYMPHOCYTE

9. Korean Patent No.:10-0324549-0000 (2002.02.01)

Title: NOVEL CYTOKINE STIMULATING B CELL PROLIFERATION AND PREPARATION METHOD THEREOF

10. Korean Patent No.:10-0355951-0000 (2002.09.26)

Title: THIF, A NOVEL STRESS-REGULATING PROTEIN WHICH INTERACTS WITH THIOREDOXIN

11. Korean Patent No.:10-372912-0000 (2003.02.06)

Title: COMPOSITION FOR TREATING MELANOMA COMPRISING IL-18 ANTISENSE CDNA

13. Korean Patent No.:10-0525704-0000 (2005.10.26)

Title: PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF GASTRIC CANCER COMPRISING INHIBITORY AGENT AGAINST 9-27 GENE

14. Korean Patent No.:10-0577318-0000 (2006.04.28)

Title: AGENT WHICH CONTAINS INHIBITORY AGENT AGAINST MIC-1 GENE, FOR THE TREATMENT OF GASTRIC CANCER, METHOD FOR THE DIAGNOSIS OF GASTRIC CANCER AND KIT FOR DIAGNOSIS

15. Korean Patent No.: 10-0535326-0000 (2005.12.02)

Title: DIFFERENTIATION REGULATING AGENT CONTAINING GENE WHICH REGULATES DIFFERENTIATION FROM STEM CELL TO NATURAL KILLER CELL AS EFFECTIVE INGREDIENT

16. Korean Patent No.: 10-0610220-0000 (2006.08.01)

Title: TRANSFORMED CELL LINE BY THE EXPRESSION VECTOR CONTAINING HUMAN VDUP1 PROMOTER AND METHOD FOR SCREENING ANTICANCER DRUG USING THEM

17. Korean Patent No.: 10-0610219-0000 (2006.08.01)

Title: METHOD FOR SCREENING CELL SIGNAL TRANSMITTER USING TRANSFORMED CELL LINE BY THE EXPRESSION VECTOR CONTAINING ADIPONECTIN PROMOTER

18. Korean Patent No.: 10-0679666-0000 (2007.01.31)

Title: MONOCLONAL ANTIBODY SPECIFIC TO HUMAN MACROPHAGEINHIBITORY CYTOKINE-1, HYBRIDOMA PRODUCING THEMONOCLONAL ANTIBODY AND DIAGNOSTIC KIT COMPRISING THEMONOCLONAL ANTIBODY

19. Korean Patent No.: 10-0729283-0000 (2007.06.11)

Title: AN AGENT FOR DIFFERENTIATING HEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL COMPRISING VDUP1 PROTEIN ORGENE EDCODING THE SAME, AND A METHOD OF DIFFERENTIATINGHEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL USINGTHEREOF

20. Korean Patent No.: 10-0860081-0000 (2008.09.18)

Title: PHARMACEUTICAL COMPOSITION FOR REGULATING THE DEGRADATION OF HIF1-ALPHA

21. Korean Patent No.: 10-0729284-0000 (2007.06.11)

Title: AN AGENT FOR DIFFERENTIATING HEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL COMPRISING vitamin D3 AND A METHOD OF DIFFERENTIATING HEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL USING THEREOF

22. Korean Patent No.: 10-0902340-0000 (2009.06.04)

Title: AN AGENT FOR DIFFERENTIATING HEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL COMPRISING YC-1 OR IL-21 AND A METHOD OF DIFFERENTIATING HEMATOPOIETIC STEM CELL INTO NATURAL KILLER CELL USING THEREOF

23. Korean Application No.: 10-2008-0049034(2008.05.27)

Title: A COMPOSITION CONTAINING OSTEOPONTIN FOR DIFFERENTIATING  
NATURAL KILLER CELL AS AN ACTIVE INGREDIENT AND A METHOD OF  
DIFFERENTIATION USING THEREOF



## **Patents (Foreign)**

1. Method for inhibiting the production of interleukin-1 or tumor necrosis factor- $\alpha$  by administrating acanthoic acid (US patent)

US patent: 5,900,434

Date issued: May 04, 1999

2. Methods for inhibiting interleukin-6 production by administrating extracts from root of *Stephania tetrandra* (US patent)

US patent: 6,162,437

Date issued: December 19, 2000

3. An agent for differentiating hematopoietic stem cell into natural killer cell composing VDUP1 protein or gene encoding the same, and a method of differentiating hematopoietic stem cell into natural killer cell using thereof

Patent Application No.: PCT/KR2005/001724

Application date: June 8, 2005

4. Differentiation regulation agent containing gene which regulating differentiation from stem cells into NK cells as effective ingredient.

US application No.: 10/597305 (US patent pending)

Application date: July 19, 2006

5. An agent for differentiating hematopoietic stem cell into natural killer cell comprising YC-1 or IL-21 and a method of differentiating hematopoietic stem cell into natural killer cell using thereof

Patent Application No.: PCT/KR2007/004816

Application date: October 2, 2007

## Publication Paper

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Exhibit B

Supplementary figure

